



## TNM FREQUENTLY ASKED QUESTIONS (FAQ'S)

The TNM Project Committee receives questions concerning the use of TNM and how to interpret rules in specific situations.

Some questions and answers are listed below by category for your convenience. These FAQs can also be found in the TNM Supplement: a Commentary on Uniform Use, 4<sup>th</sup> Edition, 2012 (edited by Ch. Wittekind, C. Compton, J. Brierley, L. H. Sobin).

**Advice on further questions may be obtained from the TNM Helpdesk by accessing the TNM Classification of Malignant Tumours page at the UICC website [www.uicc.org](http://www.uicc.org)**

## TABLE OF CONTENTS

### GENERAL QUESTIONS

AJCC versus UICC TNM .....	3
In situ carcinoma .....	3
Pathological Versus Clinical TNM .....	3
When in Doubt .....	4
R Classification .....	4
R Classification and Tis .....	5
Positive Cytology .....	5
T0 and TX .....	6
Synchronous Tumours .....	6
Simultaneous Tumours .....	7
Single Tumour Cells and Micrometastasis in Lymph Nodes .....	7
Number of lymph nodes .....	7
Pathological assessment of distant metastasis .....	8
Classification of Brain Tumours .....	8
Tumours of the Frontal and Sphenoidal Sinuses .....	8
Carcinoma of the Trachea .....	9
Carcinoma of the Urachus .....	9
Classification of primary peritoneal neoplasms .....	9
Tumour Spillage .....	9
Tumour Cells in Lymphatics .....	10
Direct Spread .....	10
N versus M .....	10
Recurrent tumour .....	11
Unknown Primary .....	11
Sentinel Lymph Node .....	11

### SITE-SPECIFIC QUESTIONS

Oral Cavity .....	12
Larynx .....	13
Thyroid Gland .....	13
Oesophagus .....	13
Stomach .....	14



Neuroendocrine Tumours .....	15
Colon and rectum .....	15
Anal Canal .....	19
Liver (Intrahepatic Cholangiocarcinoma) .....	20
Gallbladder.....	20
Bile Duct.....	21
Ampulla of Vater.....	21
Pancreas .....	21
Lung .....	22
Bone and Soft Tissue Tumours.....	29
Bone tumours .....	29
Skin Tumours .....	29
Breast .....	29
Gynaecological Tumours .....	34
Cervix Uteri .....	34
Corpus Uteri .....	34
Ovary versus Uterus.....	36
Ovary.....	36
Urological Tumours .....	37
Prostate.....	37
Testis.....	38
Kidney.....	38
Renal Pelvis and Ureter .....	39
Bladder.....	39
Urethra.....	40
<b>REFERENCES .....</b>	<b>41</b>



## GENERAL QUESTIONS

### AJCC VERSUS UICC TNM

#### *Question*

Does the AJCC classification differ from the UICC TNM classification? I am asking because I noticed that in the N classification of endometrial carcinoma, the AJCC classification reported four possible categories (NX, N0, N1, N2) and the UICC classification only three (NX, N0, N1).

#### *Answer*

Although there should be no differences in definitions and wording between the AJCC and UICC TNM classifications, unfortunately some have occurred and are mostly discussed in the 4<sup>th</sup> ed. of the TNM Supplement, one of the issues being the definition of regional lymph nodes in oesophageal and endometrial carcinoma (see TNM Suppl. p. 47, 48, 95).

### IN SITU CARCINOMA

#### *Question*

Can one stage in situ carcinoma if the regional lymph nodes have not been assessed, e.g., in a completely resected colonic polyp?

#### *Answer*

Because it is strictly NX (regional lymph nodes cannot be assessed), NX should be noted but can be assumed to be N0 because lymph node metastasis is not consistent with an in situ lesion (see TNM Suppl. p. 12).

#### *Question*

As far as I know there is no histological grading system for an oesophageal intraepithelial neoplasia. Is stage 0 (TisN0M0) enough to assign a tumour as group 0 (prognostic grouping)?

#### *Answer*

Stage 0 = TisN0M0 is sufficient to assign a case to a stage group. Consideration of a grading is not necessary. It should, however, be emphasized that the 'Tis' should only be used for high-grade intraepithelial neoplasia including carcinoma in situ.

### PATHOLOGICAL VERSUS CLINICAL TNM

#### *Question*

Does the pathological TNM replace the clinical TNM?



**Answer**

No, TNM is a dual system with a (pre-treatment) clinical classification (cTNM or TNM) and a (post-surgical histopathological) pathological classification (pTNM). Both classifications are retained unaltered in the patient's record. The former is used for the choice of treatment; the latter is used for the estimation of prognosis and the possible selection of adjuvant therapy (see TNM Suppl.p.1).

**Question**

A patient has a needle biopsy of a left upper lobe mass that is positive for squamous cell carcinoma. A computerized tomography (CT) of the thorax shows a 4 cm left upper lobe mass more than 2 cm from the carina. The clinical category is cT2. What is the pathological classification?

**Answer**

Biopsy alone is not sufficient for pathological staging in this instance. Resection of the primary tumour is needed for pT1 or pT2 lung tumours to define their limits. Biopsy, without resection, could be used, for example, for pT4 (showing invasion of the oesophagus)(see TNM Suppl. p. 148-149).

**WHEN IN DOUBT**

**Question**

I am not sure of the correct T, N or M category, e.g. because of unclear measurements, which do I select?

**Answer**

Select the lower (i.e. less advanced) category.

Example. Sonography of the liver shows a lesion suspicious but not definite for a metastasis. Select M0 (not M1) (see TNM Suppl. p. 3).

**R CLASSIFICATION**

**Question**

Does R0 mean a complete tumour-free situation or is the R classification limited to the primary?

**Answer**

R classification is not limited to the primary. The R classification not only considers locoregional residual tumour but also distant residual tumour in the form of unresected or incompletely resected metastases (R2) (see TNM Suppl. p 14).



### **Question**

If there is residual tumour after surgery, is it stage IV?

### **Answer**

RX = Presence of residual tumour cannot be assessed

R0 = No residual tumour

R1 = Microscopic residual tumour

R2 = Macroscopic residual tumour

R2 is not always synonymous with M1 (stage IV) disease. For example, in the absence of distant metastasis (M0), residual macroscopic primary tumour not or incompletely resected by the surgeon is R2.

In another example, a metastasis in the liver from a primary gastric carcinoma would be M1 (stage IV) and R2 (if the metastasis was not resected). It would be pM1 (stage IV) and R0 if the metastasis was solitary and resected with tumour-free margins (see TNM Suppl. p 14).

## **R CLASSIFICATION AND TIS**

### **Question**

Lumpectomy specimen of a breast tumour contains a 1.1 cm carcinoma with no invasive carcinoma at the resection lines; however, intraductal carcinoma was at the lateral resection line. How is this classified with respect to T category and R classification?

### **Answer**

When both an invasive and an in situ tumour are present in the same tissue, only the invasive component has to be taken into account to define the pTNM. For this case it would be pT1c and R0. Although the in situ component is not considered in the R classification, an optional solution would be R1(is) (see TNM Suppl. p. 15).

## **POSITIVE CYTOLOGY**

### **Question**

If peritoneal washing cytology, taken before any other procedure during laparotomy is positive, how do I stage the patient? Grossly visible peritoneal metastasis were not found. Is it considered a form of peritoneal metastasis and thus stage IV?

### **Answer**

Positive cytology on lavage of the peritoneal cavity performed during laparoscopy or immediately after opening the abdomen (beginning of laparotomy) corresponds to M1 (except for tumours of corpus uteri, ovary and fallopian tube). Newer data suggest that the worsening of prognosis indicated by positive lavage cytology may have been overestimated. Thus it seems important to analyze such cases separately. For identification of cases with positive cytology from pleural or peritoneal washings as the sole basis for M1, the optional addition of "cy+" is recommended, e.g. M1(cy+) and in the R classification R1(cy+) may be used (see TNM Suppl. p. 16).



**Question**

The pN and pM category demands confirmation by histology. Will confirmation by cytology be sufficient as many metastases are diagnosed by this type of specimen (fine-needle aspiration (FNA) or exudates)?

**Answer**

To confirm pM, a microscopic confirmation is requested, meaning cytological or histological confirmation. The prerequisites to use pN are listed site by site in Chapter 3 of the 4<sup>th</sup> edition of the TNM Supplement (see p. 135ff).

**Question**

If we detect isolated tumour cells after neoadjuvant therapy in the wall, e.g. of the stomach or rectum, how is this classified? (i+)?

**Answer**

The described isolated tumour cells correspond to residual viable tumour after neoadjuvant therapy. If they are found up until the muscular layer the case would be classified as ypT2. A classification as (i+) does not exist in the T category.

## **T0 AND TX**

**Question**

Explain the difference between T0 and TX.

**Answer**

TX = Primary tumour cannot be assessed  
T0 = No evidence of primary tumour

TX means you were not able to evaluate the tumour, e.g., the extent of a primary testis tumour requires radical orchiectomy; if there is no radical orchiectomy TX is used.

**Note.** cT0 means that a primary tumour was not found by any clinical methods, e.g., if you found a cervical lymph node with metastatic squamous cell carcinoma and you examined the mouth, pharynx, and larynx and found no primary tumour, you would code cT0(N1 M0) on the assumption that the primary was in the region.

## **SYNCHRONOUS TUMOURS**

**Question**

What is the rule for classifying a synchronous versus a metachronous second primary tumour?

**Answer**

If a new primary cancer is diagnosed within two months, the new cancer is considered synchronous; otherwise it is metachronous (based on criteria used by the SEER Program of the National Cancer Institute, USA). Metachronous tumours are classified separately from the preceding tumour. General rule No. 5 discusses the rules for classifying simultaneous (synchronous) tumours (see TNM Suppl. p. 5).



## **SIMULTANEOUS TUMOURS**

### **Question**

I have a case of a colon with two carcinomas, one invasive into the muscularis propria and the other invasive into the submucosa. How do I code them?

### **Answer**

T2(m) or T2(2). Where there are simultaneous (synchronous) tumours in one organ, the tumour with the highest T category is classified and the multiplicity (m) or number of tumours (2) is indicated in parentheses. If bilateral cancers occur simultaneously in paired organs, each tumour is classified independently. For carcinomas of the liver, ovary and fallopian tube, multiplicity is a criterion of T classification. If a new primary cancer is diagnosed within 2 months, the new cancer is considered synchronous (criterion of the SEER Program of the NCI, USA) (see TNM Suppl. p. 3-6).

## **SINGLE TUMOUR CELLS AND MICROMETASTASIS IN LYMPH NODES**

### **Question**

How does one classify single tumour cells detected immunohistochemically in lymph nodes?

### **Answer**

There has been considerable debate in recent years on how to classify tumour cells in lymph nodes or bone marrow that are detected by immunohistochemical or molecular methods. An optional proposal to deal with this situation is published in the 6th and 7th ed. of TNM as subsets of N0 [1, 2, 3] (see TNM Suppl. p. 9).

Single tumour cells should be distinguished from cases with morphological evidence of micrometastasis, i.e. no metastasis larger than 0.2 cm (see TNM Suppl. p. 9), These can be identified by the addition of (mi) in the cN/pN or cM/pM categories as follows:

pN1 (mi) Regional lymph node micrometastasis

pM1 (mi) Distant micrometastasis

## **NUMBER OF LYMPH NODES**

### **Question**

If less than the desired number of lymph nodes is found, and none show metastasis, should it be classified as pNX or pN0?

### **Answer**

If the examined lymph nodes are negative, but the number ordinarily resected is not met, classify as pN0. The number of lymph nodes examined and the number involved by tumour should be recorded in the pathology report. This information may be added in parentheses, e.g., for colorectal carcinoma pN0 (0/10) or pN1 (2/11) (see TNM Suppl. p. 8).



## **PATHOLOGICAL ASSESSMENT OF DISTANT METASTASIS**

### ***Question***

Should liver metastasis diagnosed by fine-needle aspiration (FNA) be considered pM1 or pMX? The primary site is the breast.

### ***Answer***

General rule 2 of TNM states : "The pathologic assessment of distant metastasis (pM) entails microscopic examination." This statement intentionally uses the term "microscopic" rather than "histologic" to allow for FNA and cytology. In this case the classification would be pM1 (see TNM Suppl. p 2).

### ***Question***

Considering that there is no longer an pMX and pM0 is only available for autopsy cases, what should we be putting on our pathology reports?

### ***Answer***

In cases in which you are informed by the clinicians about the metastasis status, you can put cM0 or cM1 on the pathology report. In cases in which you have no information, omit the 'M' and give only information about the T and N categories (see TNM Suppl. p. 10).

## **CLASSIFICATION OF BRAIN TUMOURS**

### ***Question***

The 4th ed. of TNM included a classification for brain tumours. Why has this been left out of the 5th to 7th ed.?

### ***Answer***

The application of TNM to CNS tumours has not been successful. This particularly concerns the classification as a predictor of outcome. That carries little weight compared with other factors such as histological type, tumour location and patient age (4). The N does not apply at all, and the M rarely plays a role. This field is still under study to find other means of classifying CNS tumours that will carry prognostic significance.

Further details may be obtained from the 7th edition AJCC Cancer Staging Manual [5].

## **TUMOURS OF THE FRONTAL AND SPHENOIDAL SINUSES**

### ***Question***

Current TNM classifications exist for nasal and paranasal sinuses especially for both maxillary sinus and ethmoid sinus. Is there a TNM classification for tumours of frontal and sphenoidal sinuses?

### ***Answer***

There is no TNM classification for tumours of the frontal and sphenoidal sinuses.





## **CARCINOMA OF THE TRACHEA**

### ***Question***

How is the squamous cell carcinoma of the distal trachea with invasion of the mediastinum staged?

### ***Answer***

There is no TNM classification for tumours of the trachea.

## **CARCINOMA OF THE URACHUS**

### ***Question***

Is there a TNM classification for carcinomas of the urachus? If not, should they be classified as tumours of the bladder?

### ***Answer***

There is no TNM classification for tumours of the urachus. As the criteria of the T categories are not applicable, the TNM classification of bladder tumours should not be used.

## **CLASSIFICATION OF PRIMARY PERITONEAL NEOPLASMS**

### ***Question***

How do you classify primary neoplasms of the peritoneum? We did not find any TNM classification for these tumours. Some of our colleagues use the FIGO/TNM ovary classification.

### ***Answer***

Because of the rarity of primary peritoneal neoplasms, there is indeed no TNM classification for them. Basically, there are two primary peritoneal entities: mesothelioma and primary carcinoma of the peritoneum. The latter, serous papillary carcinoma of the peritoneum, according to McCaughey et al. [6] and Killackey and Davis [7], has the same prognosis as ovarian tumours. Therefore, one could apply the TNM ovarian tumour classification until a tested scheme is available. According to FIGO rules (24th Annual Report [8]), primary peritoneal carcinoma is classified as ovarian tumours (see TNM Suppl. p. 98).

There are no proposals regarding peritoneal mesotheliomas.

## **TUMOUR SPILLAGE**

### ***Question***

If tumour is spilled into the abdomen during surgery how does this affect classification ?

### ***Answer***

Tumour spillage is considered only in the T classification of ovarian tumours. In the ovary, T1c, rupture of the capsule, includes spontaneous rupture and rupture during surgery. At other sites, it does not affect the TNM or stage grouping (see TNM Suppl. p 98).



## **TUMOUR CELLS IN LYMPHATICS**

### ***Question***

If I have a carcinoma of the colon with invasive tumour in the submucosa, but with lymphatics in the muscularis propria containing tumour cells, which do I select, T1 or T2?

### ***Answer***

T1 (submucosa). The microscopic presence of tumour cells in lymphatics or veins does not qualify as local spread in the T classification (except for liver, testis and penis). The optional L(ymphatic) and V(enous) classifications can be used to record such involvement (see p. 17, TNM 7th ed. [2]).

## **DIRECT SPREAD**

### ***Question***

Is a tumour that has spread directly from a gastric primary into an adjacent regional lymph node coded in the T or N category?

### ***Answer***

N category. Direct spread into a regional lymph node is classified as lymph node metastasis; direct spread into an adjacent organ, e.g., the liver from a gastric primary, is recorded in the T classification (see TNM 7th ed. [2], p. 12).

## **N VERSUS M**

### ***Question***

For gastric carcinoma, when we find tumour nodules in the omentum, should we classify them as lymph node metastasis?

### ***Answer***

Unless the nodules are in the lymphatic drainage region (regional lymph nodes) they should be considered distant metastasis and classified cM1 or pM1. (See TNM 7th ed. [2], p. 75).



## RECURRENT TUMOUR

### *Question*

How can I classify a patient who had an apparently complete local excision of a carcinoma of the rectum, but was found, 2 years later, to have recurrent tumour at the same site?

### *Answer*

Use the Recurrent tumour, r symbol. There must be a documented disease-free interval to use this symbol. For example, rcT0N0M0 would designate the status during the disease free interval and rcT1N0M0 would indicate a recurrent tumour at the primary site (estimated clinically to be in the submucosa). After a second resection the result might be expressed as: rpT2pN1 rcM0, if the resected tumour was found pathologically to be in the muscularis propria (see TNM Suppl. p. 20).

In other cases, the recurrence in the area of the primary tumour may be indicated by "rT+".

**Example:** Local recurrence after simple mastectomy, 2 cm in greatest dimension, with or without invasion of skin or chest wall: rT+

### *Question*

A patient has a primary resected and it is classified as pT3pN1 cM0 (e.g. colorectal carcinoma). Then 1 year later he developed metastatic disease, what is the correct TNM classification? T3N1 M1?

### *Answer*

The correct staging at the time of recurrence would be rcT0N0M1 provided no recurrent primary tumour or regional lymph node metastasis are present. The original TNM status is not considered in a recurrent tumour.

## UNKNOWN PRIMARY

### *Question*

How do I classify a patient who has metastatic melanoma in a cervical lymph node less than 3 cm in greatest dimension without a known primary or other metastasis?

### *Answer*

cT0pN1cM0, stage III. The staging is based on regional lymph node and/or distant metastasis status. In this case, the site of metastasis is assumed to be regional (see TNM Suppl. p. 22).

## SENTINEL LYMPH NODE

### *Question*

How do I classify sentinel lymph node status?

### *Answer*

The following is applicable when sentinel lymph node assessment is attempted (see TNM Suppl. p. 10) :

pNX(sn) = Sentinel lymph node could not be assessed  
pN0(sn) = No sentinel lymph node metastasis  
pN1(sn) = Sentinel lymph node metastasis



**Question**

How are isolated tumour cells or micrometastasis staged in regional lymph nodes of colorectal carcinoma?

**Answer**

Isolated tumour cells (ITC) as defined in the actual TNM classification [2] (p. 13-15) are classified as pN0(i+). Micrometastases are classified as pN1 mi, if only one regional lymph node is involved. The TNM system does not recommend any techniques or procedures to obtain a maximum of findings. It is, however, generally accepted that step sectioning of lymph nodes with consecutive immunohistochemistry is not necessary to detect ITC or micrometastasis.

**Question**

To classify a case as V1 or V2 do we have to demonstrate tumour cells in the lumen of the vessel, or is an invasion sufficient to classify as V1 or V2?

**Answer**

Invasion of vessel wall is sufficient to classify as V1 or V2 (see TNM Suppl. p. 21).

## SITE-SPECIFIC QUESTIONS

### ORAL CAVITY

**Question**

What is the definition of the 'masticator space'?

**Answer**

The masticator space (MS) is the lateral anatomical region below the middle cranial fossa and is defined by distinct fascial planes. The main fascial boundary is related to the superficial layer of the deep cervical fascia. This is also known as investing fascia. The investing fascia is formed when the superficial layer of the deep cervical fascia splits at the lower margin of the body of the mandible and rises to enclose the muscles of mastication. Medially the fascia combines with another fascia, the interpterygoid fascia, and then rises up to the skull base. Laterally, the fascia rises up above the level of the zygomatic arch and covers the temporalis muscle. The zygomatic arch is used to subdivide the MS into a suprazygomatic MS (portion above the zygomatic arch) and the naso pharyngeal MS (portion below the level of the zygomatic arch). The contents of the MS include the mandibular division of the 5<sup>th</sup> cranial nerve, the muscles of mastication, sections of the internal maxillary artery, the pterygoid plexus and the ramus and coronoid of the mandible. For lesions related to the lower alveolus, these would be related to the most inferior part of the masticator space that is enclosed by the investing fascia [9] (see TNM Suppl. p. 30-31).



## LARYNX

### **Question**

Since the T classification of laryngeal tumours involves assessment of vocal cord fixation, does it mean that pT is not possible without such information given by the clinician?

### **Answer**

For pathological classification concerning impaired mobility or fixation of vocal cords, the information from the clinical T is used for the pathologic T. This is in accordance with TNM rule No. 2, pathological classification "is based on the evidence acquired before treatment, supplemented or modified by the additional evidence acquired from surgery and from pathological examination". So, indeed, if the information concerning presence or absence of vocal cord fixation is lacking, it may be impossible to determine the pT (see TNM Suppl. p. 42).

### **Question**

A total laryngectomy specimen including six tracheal rings of cartilage, what would a paratracheal lymph node towards the distal end of the trachea (below the thyroid cartilage and the thyroid) be regarded as? Would this still be considered a cervical lymph node and if so what level?

### **Answer**

It is an unusual situation. In the TNM Suppl. 4<sup>th</sup> ed. (see p. 118), the regional lymph nodes of head and neck carcinomas are described and listed. The paratracheal lymph nodes are included and should therefore be considered regional and are included in Level VI.

## THYROID GLAND

### **Question**

How do I stage a papillary carcinoma of the thyroid that has a small lymph node attached to the thyroid and focally involved by the papillary carcinoma?

### **Answer**

The problem is addressed in the TNM booklet, 7th ed. [2], p.12: Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis. Thus the case is classified as pN1a. If it is not evident from the resection specimen, the surgeon has to mark the removed lymph node(s) to allow the pathologist to distinguish between pN1a and pN1b.

## OESOPHAGUS

### **Question**

Is a tumour of the oesophagus with invasion of perioesophageal fatty tissue without infiltration of adjacent structures classified as pT3 or pT4? Does the perioesophageal fatty tissue belong to the mediastinum and thus to adjacent structures?

### **Answer**

The described situation is classified as pT3. The fatty tissue belongs to the adventitia and not to adjacent structures such as bronchus, heart, pericardial sac and aorta (see TNM Suppl. p. 47).



**Question**

The present definition of regional lymph nodes in oesophageal cancer is not very precise. How are the lymph nodes enumerated according to the Japanese nomenclature classified with regard to regional lymph nodes or distant metastasis?

**Answer**

A list of the lymph nodes with numbers of the AJCC classification [5] is shown on p. 47 and 48 of the TNM Suppl.. Other involved lymph nodes are classified as distant metastasis.

**Question**

Should we use the prefix 'y' for tumours in oesophagectomy specimens that have previously been treated by endomucosal resection (EMR)?

**Answer**

EMR does not qualify for the prefix 'y'.

The 'y' symbol should be used in cases in which classification is performed during or following multimodality therapy (see TNM Suppl. p. 18).

**Question**

With the new 7th ed. TNM [2] staging of oesophageal tumours, are coeliac and supraclavicular lymph nodes considered regional for upper, mid- and lower oesophageal tumours?

**Answer**

Coeliac lymph nodes are considered regional (N1-N3 depending on the number of involved lymph nodes) and metastasis in supraclavicular lymph nodes are classified as cM1 or pM1 if microscopically confirmed (see TNM Suppl. p. 48).

**Question**

Do you classify coeliac axis or left gastric artery nodes as M1 or N for an oesophageal cancer that involves the lower 5 cm of the oesophagus and spreads to the proximal 2 cm of the stomach with no other sites of disease apart from perioesophageal or perigastric nodes?

**Answer**

Direct spread to the stomach by an oesophageal tumour makes the lymph nodes of the stomach regional, and therefore they should be classified in the N classification (depending on number of involved lymph nodes) and not in cM1/pM1 (see TNM Suppl. p. 47-48).

## **STOMACH**

**Question**

A post-chemotherapy gastrectomy case with signet-ring cell carcinoma shows one clearly positive lymph node. Immunohistochemistry has been performed, which showed one positive cell in five other regional lymph nodes. How to classify this case ?



**Answer**

The one positive regional lymph node is classified as ypN1. It seems difficult to classify the other findings. Strictly, these findings should be classified as isolated tumour cells ITC and should not be considered in the N classification. On the other hand this might represent regressive changes of lymph node metastasis after chemotherapy and should then be classified as ypN2.

I think you have to invoke Rule No. 4 (see TNM Suppl. p. 3), if in doubt use the lower stage i.e. ypN1.

**Question**

How should I classify a supraclavicular lymph node metastasis of a signet-ring cell carcinoma of the stomach (N or M category) ?

**Answer**

The supraclavicular lymph node metastasis is classified as pM1 LYM or pM1 LYMPH (see TNM Suppl. p. 53).

## **NEUROENDOCRINE TUMOURS**

**Question**

How do I classify a 3 cm primary well-differentiated endocrine tumour of the small bowel with a mesenteric mass (lymph node metastasis)?

**Answer**

This case is classified as pT2pN1 cM0, if there are no distant metastases. It is not especially indicated if there is only one lymph node metastasis or a mass that might correspond to several matted lymph node metastases (see TNM Suppl. p. 60).

**Question**

How shall I classify a well-differentiated neuroendocrine carcinoma of the appendix (malignant carcinoid) with spread into mesoappendix ? Is it pT3 (like adenocarcinomas)?

**Answer**

Carcinoids of the appendix have their own TNM classification (from the 7<sup>th</sup> ed. [2]). Invasion of the meso-appendix is a feature of only the ENETS TNM-classification but not of the IUCC/AJCC TNM classification for carcinoid tumors of the appendix (see TNM Suppl. p. 57-58).

## **COLON AND RECTUM**

**Question**

In carcinoma of the colon is a tumour that has reached the serosal surface classified as pT3 or pT4? What is the definition of reaching the serosa? In some places it is taken to be tumour that is within 1 mm of the serosal surface.

**Answer**

T3 covers tumours in the subserosa, i.e., those beneath the serosal surface.

T4 applies to tumours that "perforate visceral peritoneum", i.e., the serosal surface (see TNM Suppl. p. 62).



**Question**

I have a carcinoma of the sigmoid colon extending into the submucosa. In a vein in the pericolic fat there is a tumour thrombus. Metastasis is present in one of eight regional lymph nodes. How should this case be staged?

**Answer**

The case is classified as pT1pN1a(1/8) cM0,V1. Venous invasion is neither considered in the T nor in the N category (see TNM Suppl. p. 63).

**Question**

In adjuvant trials on colorectal carcinomas we make the distinction between T4a and T4b tumours as being the following:

T4a = Invasion of other organs

T4b = Penetration of the serosa

How is the distinction made in the TNM Supplement?

**Answer**

In the 7th ed. of the TNM classification [2], the definitions of the subcategories have changed compared with the TNM Supplement, 3rd ed. [10]. The definitions are:

T4 Tumour perforates visceral peritoneum and/or directly invades other organs or structures

T4a Tumour perforates visceral peritoneum

T4b Tumour directly invades other organs or structures\*

**Notes.**

\*Direct invasion in T4b includes invasion of other organs or segments of the colorectum by way of the serosa, as confirmed on microscopic examination, or for tumours in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria.

Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1-3, depending on the anatomical depth of wall invasion (see TNM Suppl. p. 62-63).

**Question**

In a patient with adenocarcinoma of the colon there was full-thickness penetration of the wall, 13 positive nodes and also a "free-floating" focus of carcinoma in the peritoneal cavity. No other peritoneal tumour was found. Should that be staged as T0, TX or T1?

**Answer**

The case should be considered pM1, because there was tumour in the peritoneal cavity separate from the primary. The primary tumour would be pT3, or if it penetrated the serosa, pT4, and pN2 because of the number of nodes involved (see TNM Suppl. p. 62-63).





**Question**

How do I classify a carcinoma in a diverticulum of the sigmoid colon with penetration of the muscularis propria and penetration into the pericolic fat? The diverticulum is lined by a thin fibrous membrane. There are 31 regional lymph nodes without metastasis and no distant metastasis.

**Answer**

The case should be classified as pT3pN0(0/31) cM0.

**Question**

In the 7th ed. of the TNM classification [2], tumour deposits (TD) are recorded as a site-specific factor. It appears that they do not affect the N classification unless no lymph nodes are involved, in which case it is designated as N1c. How would you classify a tumour that has three involved lymph nodes and four tumour deposits without lymphoid tissue? Would it be N1bTD4?

**Answer**

The case you describe is classified as pN1b. The TDs should be separately counted (see TNM Suppl. p. 63-64). It may sometimes be difficult to count TDs correctly. As to that issue, please refer to the TNM booklet [2], p. 103. In addition, you have to be sure that TDs are not lymph node metastasis.

**Question**

Do pericolic TD correspond to positive regional lymph nodes in colorectal carcinoma or is cN1c/pN1c used only in the absence of lymph node metastasis?

**Answer**

cN1c/pN1c is used **only** in the absence of regional lymph node metastasis (see TNM Suppl. p. 64).

**Question**

Is a rectal carcinoma that extends into the anus a T3 or a T4?

**Answer**

The TNM Supplement states that: "Intramural direct extension from one subsite (segment) of the colon to an adjacent one is not considered in the T classification. The same applies to intramural direct extension from the rectum to the anal canal". The T category is determined by the depth of the invasion (see TNM Suppl. p. 62).

**Question**

Is a rectal carcinoma infiltrating the levators to be considered T3 or T4?

**Answer**

We suggest coding a rectal carcinoma infiltrating the levators as T4b (invasion of adjacent structures) (see TNM Suppl. p. 63). This is based on

- The poor prognosis
- Difficulty in achieving an R0 state (no residual tumour)
- Radical surgery required



**Question**

I have a rectal carcinoma below the peritoneal reflection that perforates the mesorectal fascia but does not affect peritoneal serosa. Is this a pT3 or pT4 tumour?

**Answer**

pT3 seems to be correct.

We have no data to classify the perforation of the mesorectal fascia as cT4/pT4.

**Question**

Does a serosal penetration in a colonic adenocarcinoma influence R classification? There are no known clinical metastases and the tumour free margin of the mesocolic resection is more than 1 mm.

**Answer**

The perforation of a colorectal carcinoma is not considered in the R classification, e.g. if other resection margins are without tumour invasion the case can be classified as R0.

**Question**

I received a colon tumour, which is a moderately differentiated adenocarcinoma and approximately 50% at most mucinous. I was able to find multiple mesenteric lymph nodes that are negative for tumour. However, three of the lymph nodes had mucinous pools in them. Despite multiple serial sections of at least three levels, I could find no atypical cells. I feel that I cannot call these pools of mucin metastatic tumour, even though I believe the mucin is from the lesion. I have made note of the mucin in the report, but I am unsure how to classify these lymph node findings. What is the current consensus concerning this type of lesion under these circumstances?

**Answer**

The TNM approach depends on whether there has been neoadjuvant therapy. If the surgery was done after neoadjuvant therapy, mucin pools without tumour cells in the bowel wall or lymph nodes are not considered positive for tumour. If there has been no neoadjuvant therapy, mucin pools are considered positive for tumour.

**Question**

We have a patient who had mucinous adenocarcinoma of the rectum. After neoadjuvant therapy we could find mucinous masses only in the intestinal wall and in three of 19 regional lymph nodes, no distant metastasis clinically. How is this case classified according to TNM?

**Answer**

This case (after neoadjuvant therapy) is classified as ypT0pN0(0/19) ycM0. Mucinous masses without viable tumour cells are not considered in the ypT and ypN classification (see TNM Suppl. p. 18).

**Question**

I have a rectal mucinous adenocarcinoma (pT3) and metastasis to one of 16 regional lymph nodes (pN1a). An additional lymph node with metastasis was received located at the pelvic wall. Should this lymph node metastasis be considered among the regional lymph nodes or is it a distant metastasis?



**Answer**

The lymph node localization might be interpreted as lateral sacral or mesorectal. Therefore, this lymph node metastasis being regional would change the classification to pT3pN1b(2/17) cM0, Stage IIIB.

**Question**

In a colon carcinoma with invasion of the Gerota fascia but not the kidney, is this T3 or T4?

**Answer**

Gerota fascia should be considered an adjacent structure and should therefore be classified as pT4b.

**Question**

For rectal adenocarcinoma that is invading beyond the muscularis propria but not involving lymph nodes, would invasion of the anal skin (undermining the anal squamous epithelium close to the distal excision margin) upstage the tumour from pT3 to pT4?

**Answer**

If no sphincter structures are involved the case should be classified as cT3/pT3.

**Question**

Which R Classification is appropriate to describe intraoperative tumour perforation in resection of rectal cancer, if macroscopically and microscopically the tumour is completely removed?

**Answer**

It is classified as R0. The T category is not implied by intra-operative perforation. Perforation should be documented separately because of the poorer prognosis of patients.

## **ANAL CANAL**

**Question**

I have a case of an anal carcinoma that falls into the ypT2 category. There is one perirectal and one external iliac lymph node positive. The external iliac lymph node has been separately sent by the surgeon. Is a metastasis in this lymph node classified as N1, N3 or M1 ?

**Answer**

According to the definition of the regional lymph nodes of tumour of the anal canal, metastases in external iliac lymph nodes are considered distant metastases and should be classified as cM1/pM1 (see TNM Suppl. p. 121).



## **LIVER (INTRAHEPATIC CHOLANGIOCARCINOMA)**

### **Question**

If an intrahepatic cholangiocarcinoma invades through the liver capsule into the retroperitoneum, is the tumour classified as a T4?

### **Answer**

An invasion of the retroperitoneum would correspond to a perforation of the visceral peritoneum and would be classified as cT3/pT3 (see TNM Suppl. p. 145).

### **Question**

What is the definition of the periductal growth in intrahepatic cholangiocarcinoma classified as cT4/pT4?

### **Answer**

Primary periductal growth in intrahepatic cholangiocarcinoma is a rare entity (less than 10%). These tumours show a primary periductal frequently multifocal growth, practically never mass-forming. Affected patients have a very poor prognosis thus cT4/pT4 is justified (see TNM Suppl. p. 66).

### **Question**

A patient with intrahepatic cholangiocarcinoma has metastasis in para-aortic lymph nodes. Is this finding classified as N1, N2 or M1?

### **Answer**

The definition of the regional lymph nodes for right-liver and left-liver intrahepatic cholangiocarcinoma is shown on p. 114 of the TNM booklet. It does not include para-aortic lymph nodes, involvement of which should therefore be classified as cM1 or pM1 if microscopically proven. Neither in the UICC [2] nor in the AJCC classification [5] is a definition of N2 lymph nodes provided.

## **GALLBLADDER**

### **Question**

In the case of a gallbladder carcinoma, a partial hepatectomy specimen was submitted that showed an invasion of liver parenchyma and about 1.5 cm away from the invasion a 0.4 cm nodule without macroscopic or microscopic connection to the invasive tumour. How should this nodule be classified?

### **Answer**

This nodule should be classified as pM1.



## **BILE DUCT**

### **Question**

In a case of perihilar cholangiocarcinoma (Klatskin tumour) with direct (per continuitatem) invasion of the pancreas, how is this finding classified?

### **Answer**

Although the invasion of the pancreas is not explicitly mentioned in the T categories of perihilar tumours (=Klatskin tumours), it is recommended to use the definition of TNM of the distal bile duct tumours and thus this case should be classified as pT3.

### **Question**

Do I stage a carcinoma of the distal common bile duct occurring in the intrapancreatic portion of the bile duct as pancreatic or bile duct tumour?

### **Answer**

The described tumour is classified according to the classification of distal extrahepatic bile duct tumours.

## **AMPULLA OF VATER**

### **Question**

We have an ampullary adenocarcinoma that has infiltrated beyond the duodenal wall but not in the pancreatic parenchyma. Is this T2 or T3?

### **Answer**

Assuming that the tumour you describe has invaded (peripancreatic) soft tissues, the case is classified as cT4/pT4 (see TNM Suppl. p. 146).

## **PANCREAS**

### **Question**

A ductal carcinoma of the pancreas measuring 5 cm in greatest dimension involving the head and body of the pancreas, does not show extrapancreatic extension but it invades the common bile duct within the head of the pancreas. There is one pancreatoduodenal and one common bile duct lymph node positive for metastatic carcinoma of 16 examined lymph nodes. Is this a T2N1 or T3N1 tumour?

### **Answer**

The case is classified as pT3pN1 cM0. Please refer to p. 146 of the TNM Supplement.



**Question**

Should a ductal carcinoma of the pancreas with invasion of the superior mesenteric vein be staged as cT4/pT4?

**Answer**

Although it is not mentioned in the definition of the T4 category of pancreatic tumours, involvement of the superior mesenteric vein should be classified as cT4/pT4 (see TNM Suppl. p. 68).

**Question**

I have seen the list of regional lymph nodes for pancreatic cancer resections in the TNM 6th ed. book. However, it is not entirely clear when a node is far enough away from the pancreas to be classed as M1 if involved. For example, our surgeons often send us hepatic artery nodes, coeliac axis nodes and aorto-caval nodes separately. Would any or all of these groups be classified as cM1/pM1 if involved (i.e. rather than N1) ?

**Answer**

Hepatic artery nodes might be considered equivalent to common bile duct nodes = regional = cN1/pN1

Coeliac axis nodes = regional for tumours of the head only = cN1/pN1

Aorto-caval nodes = distant metastasis = cM1/pM1 (see TNM Suppl. p. 120-121).

## **LUNG**

**Question**

Does the new 7th ed. TNM classification [2] for lung cancer cover all lung cancers including small cell lung cancer?

**Answer**

The classification applies to carcinomas of the lung including non-small cell carcinomas, small cell carcinomas and bronchopulmonary carcinoid tumour (see TNM Suppl. p. 69).

**Question**

For lung carcinomas, does T2 invasion of visceral pleura mean perforation of pleural membrane?

**Answer**

T2 invasion of visceral pleura includes either of the following:

- tumour reaches the elastic membrane of the visceral pleura
- tumour is present on the surface of the visceral pleura (see TNM Suppl. p. 71)



**Question**

If a lung tumour that is <3 cm (2.8 cm) in maximum dimension with no visceral pleural invasion involves the bronchus intermedius, is it a T1 or a T2 tumour?

**Answer**

Bronchus intermedius should not be considered as part of the right main bronchus. The correct classification for the described tumour therefore is cT1b/ pT1b.

**Question**

Regarding the T classification of lung carcinoma, if a tumour is 3 cm and grows by direct invasion through a fissure to involve by direct invasion the adjacent lobe, does it become a T2 or T4?

**Answer**

A tumour with local invasion of another lobe without tumour on the pleural surface should be classified as T2, in the 7th ed. [2] cT2a/pT2a (see TNM Suppl. p. 72). This classification is trumped if other features such as size dictate a higher T category to be applied.

**Question**

How do I classify a patient with a 2 cm primary adenocarcinoma of the RUL of lung with multiple deposits of adenocarcinoma in the RLL, negative lymph nodes and no other metastasis.

**Answer**

This is classified as T4 (separate tumour nodules in a different lobe) and as the secondary tumour was histologically confirmed, it is pT4 (see TNM Suppl. p. 71).

**Question**

Please define 'mediastinum' in lung cancer being classified as T4 as opposed to mediastinal pleura being classified as T3. In addition, intrapericardial resection with tumour in the fat underneath the parietal pericardium but not infiltrating the pericardial fibrous tissue, how is this T categorized?

**Answer**

Until the 4th ed. published in 1987 and 1992 [11], the highest T category was 'T3' and this included the descriptor 'mediastinal invasion.' In the 5th ed. [12], the T4 category was reintroduced and invasion of the mediastinum and contents were divided between 'T3' and 'T4.' 'Mediastinal pleura' and 'parietal pericardium' remained 'T3,' whereas invasion of 'heart,' 'great vessels,' etc., became 'T4.' My interpretation has been that 'mediastinum' was retained, and assigned to the new T4 category, to cover all the contents that were not specifically assigned to 'T3' or 'T4,' i.e. mediastinal fat, connective tissue, thymus, etc. We assume that by describing invasion into the fat 'underneath' the parietal pericardium, you mean 'superficial' to the pericardium as this is the only context in which fat could be invaded without pericardial invasion. If this assumption is correct then the case should be classified as 'T4' (see TNM Suppl. p. 72).



**Question**

For clinical staging of lung cancer: do we need to measure the tumour size on the lung 'window' or on the mediastinal 'window' of CT scans?

**Answer**

Perform the measurement on the 'window' that is most accurate in your institution. Presumably, a diagnostic radiologist would be able to indicate which is the most accurate procedure.

**Question**

I have an acinar adenocarcinoma of the lungs, which shows large areas with a bronchoalveolar growth pattern. In the resection specimens there are foci of bronchoalveolar carcinoma away from the original tumour. Should this be counted as a synchronous tumour or simply part of the first tumour?

**Answer**

The case you describe would be classified as cT3/pT3, provided the foci are in the same lobe and there is non-tumourous tissue between the different foci. If the tumour nodules occur in another lobe the case would be classified as cT4/pT4, or cM1a/pM1a if in the contralateral lung (see TNM Suppl. p. 71).

**Question**

Lung cancer invading 'great vessels' is classified as T4. How are 'great vessels' defined and where is the 'cut-off'? Does a large pulmonary arterial branch in a lobectomy specimen qualify as a great vessel or does it refer only to the main pulmonary artery and aorta?

**Answer**

The definition of the great vessels are given on p. 72 in the TNM Supplement.

- Aorta
- Superior vena cava
- Main pulmonary artery (pulmonary trunk)
- Intrapericardial portions of the right and left pulmonary artery
- Intrapericardial portions of the superior and inferior right and left pulmonary veins.

Invasion of more distal branches does not qualify for classification as T4.





**Question**

1) If there are two adenocarcinomas in the same lobe, but they have very different histologies (for example a well-differentiated papillary adenocarcinoma, and a poorly differentiated signet-ring cell carcinoma, both TTF-1+ and proven to be of lung origin), according to the guidelines in the AJCC manual, as these are both 'adenocarcinomas' they should be staged as T4. However, I'm hesitant to do this, because at least at the histological (and probably genetic) level, the tumours are quite distinct. How would you stage this situation?

2) If a patient has two tumours in the same lobe, and one is a bronchioloalveolar carcinoma and the other is an adenocarcinoma, would these be staged as separate primaries?

3) If a patient has two BACs, but one is clearly mucinous, and the other is non-mucinous, do you stage these as separate primaries?

**Answer to 2)**

No, they would be staged as T3 (two tumour foci in the same lobe).

**Answer to 1) and 3)**

I have consulted our pulmonary pathologist and the examples that you have given could all be considered separate primaries. Therefore, one would classify the more advanced in each group and indicate that there were two primaries by putting (2) after the T, e.g. T2(2) (see TNM Suppl. p. 71).

**Question**

How is the invasion of the 'mediastinum' as a criterion for cT4/pT4 defined?

**Answer**

'Mediastinum' was assigned to the T4 category to cover all of the contents that were not specifically mentioned, e.g. mediastinal fat, connective tissue, thymus, etc.

**Question**

Referring to the lung, I have a specimen with a 7 cm adenoca in which there is a separate 1 cm subpleural adenoca that is only about 1 cm from the larger mass. The lesions are in the same lobe. There is no definite contiguity between the lesions macro- or microscopically. Is this a T4 tumour?

**Answer**

The case you describe is classified as cT3 or pT3 (see TNM Suppl. p. 71).

**Question**

I have a 2.5 cm invasive bronchial adenocarcinoma with prominent non-mucinous bronchioloalveolar CA features, far enough away from the carina. One of the BAC-like foci has a prominent nested component of alveolar oedema/mucin involving the elastic layer of the pleura, but only scattered foci of tumour lining septae are present, well away from the pleura. Is this T1 or T2?

**Answer**

The case you describe should be classified as cT1/pT1. In the TNM Supplement, 3rd ed. (p. 48) [10], it is stated: Invasion of visceral pleura (T2) includes not only perforation of the mesothelium but also invasion of the lamina propria serosae.

I conclude from your description that this criterion has not been fulfilled.



### **Question**

How does one classify a patient with a tumour obstructing the right main bronchus, in which the resultant collapse/consolidation of the middle and lower lobes obscures the margins of the tumour and one cannot assess its size?

### **Answer**

The features described suggest that the tumour is at least T2, but one cannot assess size to determine if it is T2a, T2b or T3. One should apply General Rule No. 4 (see TNM Suppl. p. 3) in such circumstances. This states that 'If there is doubt concerning the correct T, N or M category to which a particular case should be allotted, then the lower (i.e. less advanced) category should be chosen. This will be reflected in the stage grouping.' This case should be classified as cT2a, and if node-negative is Stage IB.

### **Question**

How should one classify a patient with a 4 cm spiculated lesion in the left lower lobe, and a 2 cm lesion in the right upper lobe? A needle biopsy from the left lesion confirms adenocarcinoma. On positron emission tomography (PET-scan) there is high uptake in both of the lung lesions but no uptake elsewhere in the hilum, mediastinum or at distant sites. Does one need to biopsy the right lesion to confirm that it is of different cell type?

### **Answer**

Whether or not a needle biopsy of the right lung lesion should be undertaken in this case depends on whether the treatment approach proposed by the multidisciplinary team would be influenced by the differing interpretations of the classification on the evidence so far available. This case could be classified as, cT2a N0 M1a, Stage IV if the smaller lesion is considered a metastasis. If, however, the two lesions are shown to be synchronous primary tumours, they should be classified under General Rule No. 5 (see TNM Suppl. p. 3-4), which states that 'in the case of multiple simultaneous tumours in one organ (the two lungs are considered to be a single organ for these purposes), the tumour with the highest T category should be classified and the multiplicity or the number of tumours should be indicated in parenthesis' as cT2a(m)N0M0 or cT2a(2)N0M0, stage IB. If treatment decisions would be influenced by knowing the cell type of the right-sided lesion, which might show a different cell type or provide morphological, immunohistochemical or molecular differences suggesting that the tumours are different subtypes of the same cell type, then a needle biopsy of the right-sided tumour would be justified for staging purposes.

### **Question**

How should one classify a case in which an undifferentiated carcinoma of the left upper lobe is infiltrating the soft tissues of the chest wall. There is a positive lymph node adjacent to the chest wall lesion and no intrathoracic node involvement. Is this pM1 or pN1, if one considers the soft tissue as an infiltrated organ and the local node as a regional node?

### **Answer**

In answering this question one has to assume that clinical and pathological features have excluded this tumour being a soft-tissue primary (sarcoma) or a breast carcinoma. If this is so, then the TNM Supplement advises (see p. 7-8): 'In rare cases, one finds no metastases in the regional lymph nodes, but only in lymph nodes that drain an adjacent organ directly invaded by the primary tumour. The lymph nodes of the invaded site are considered as those of the primary site for N classification.' Lymph nodes in the soft tissues of the chest wall nodes are not considered 'regional' lymph nodes in lung cancer and hence the classification to be applied should be 'pM1b'.



**Question**

A case of lung cancer is classified on clinical/pre-treatment assessment as cN0 or cN1. At surgery it is deemed to be irresectable because of extensive mediastinal invasion by the primary tumour. The pathologist can only confirm that resected/sampled mediastinal nodes from stations 4 and 7 are clear of disease. Should this case be classified as pNX, pN0 or pN1?

**Answer**

The TNM classification sets prerequisites for the number and distribution of lymph nodes that are required to be examined histologically to establish the pN category. In lung cancer these prerequisites are: 'Histological examination of hilar and mediastinal lymphadenectomy specimen(s) will ordinarily include six or more lymph nodes/stations. Three of these nodes/stations should be mediastinal, including the subcarinal nodes (#7) and three from N1 nodes/stations (see TNM Suppl. p. 135).' However, if all the lymph nodes examined are negative, but the number or distribution of the lymph nodes recommended to be ordinarily examined is not met, classify as pN0 (see TNM Suppl. p. 8). The combination of, for example, a pathologically confirmed pT4 with pT4pN0 cM0 would not fulfill the criteria necessary to establish a pathological stage and this case should be classified as clinical stage IIIA.

**Question**

A patient underwent a wedge resection of the right upper lobe for a pT1N0 cM0 adenocarcinoma. Six months later a further tumour was discovered in the right upper lobe and the patient underwent completion upper lobectomy. The pathological examination of the surgical specimen showed that the new lesion was a metastasis within an intrapulmonary lymph node, and lymph node tissue was clearly seen with a capsule at the periphery of the new tumour. How should one classify this case?

**Answer**

This should be classified as recurrent tumour in a lymph node and not as a new primary. It would be appropriate to classify this as rpT0pN1 rcM0 (see TNM Suppl. p. 20).

**Question**

A patient underwent right upper lobectomy with systematic nodal dissection. Pathological examination showed a pT1 adenocarcinoma and confirmed that the requirements for a full pathological examination of the lymph nodes had been met. We confirmed involvement of the interlobar lymph node station and found metastasis in lymph nodes (#12) with no other deposits in N1 and N2 stations, except for isolated tumour cells (ITC) in a paratracheal station (# R4). Should we classify this case as pN1, pN0(i+) or pN2(i+)?

**Answer**

The TNM supplement only considers ITC as a subcategory of the pN0 classification. Unfortunately, if one assigned the category of pN0(i+) or created a new one of pN2(i+) the irrefutable evidence of pN1 disease would be obscured. We can only suggest that the case be classified as pN1.

**Question**

Our surgeon undertook right upper lobectomy and resection of the fused apical segment of the right lower lobe in a patient following induction chemotherapy. Macroscopically, the tumour is 3.5 cm in size and appears to involve the attached segment. However, on microscopy I cannot identify the visceral pleura of the oblique fissure to confirm invasion. How should one classify this case?



**Answer**

The use of an elastin stain may facilitate the identification of the visceral pleura (see TNM Suppl. p. 71). However, direct invasion of an adjacent lobe, even when the fissure is deficient and there is no pleural separation at the point of invasion is classified as T2 (see TNM Suppl. p. 72). This case should be classified as ypT2a.

**Question**

On pathological examination of a resection specimen, there is a 6 cm tumour with direct invasion into hilar fat. Is hilar fat considered evidence of mediastinal invasion or does this qualify as invasion of the mediastinal pleura? Is this categorized as pT2b, pT3 or pT4?

**Answer**

Invasion of hilar fat is not included in any of the present T descriptors and we have no data on which to give advice. In this case there needs to be a dialogue between the surgeon and the pathologist. If the surgeon undertook a lobectomy and was certain that the resection margins were clear of disease, and if the pathologist confirms an R0 resection, then one can be reasonably sure that the 'hilar' fat is truly hilar and one could assign the pT2b category to this case (see TNM Suppl. p. 72). If a pneumonectomy had been performed, then there would be real concern that the 'hilar' fat is really 'mediastinal' fat. If the discussion between the pathologist and the surgeon concluded that this was the case, then the pT4 category should be assigned. Further discussions would no doubt centre on whether this constituted an R1 resection!

**Question**

Pathological examination of a resection specimen has shown a 2.5 cm peripheral adenocarcinoma, which involves the visceral pleura but does not extend through to the superficial surface of the pleura. Should this be classified as pT1b or pT2?

**Answer**

Invasion of the visceral pleura is a T2 descriptor and is defined as 'invasion beyond the elastic layer including invasion to the visceral pleural surface.' The use of elastic stains is recommended when this feature is not clear on evaluation of H&E sections (see TNM Suppl. p. 71). If in this case the invasion extends beyond the elastic lamina, the case should be classified as pT2a.

**Question**

Clinical classification suggested that our patient had a cT2N2M0 non-small cell lung carcinoma (NSCLC). Pre-operative biopsy of ipsilateral mediastinal nodes confirmed N2 disease and thoracotomy was not undertaken. Should this case be classified as cN2 or pN2? Should this case now be assigned a pathological stage?

**Answer**

Microscopical confirmation of the nodal disease would allow this to be classified as cN2 (see p. 1-2). However, to be designated a pathological stage, the primary tumour has also to be classified. If resection of the tumour is not possible, one can calculate the T category after a biopsy adequate to evaluate the highest pT category (see TNM Suppl. p. 70).



## **BONE AND SOFT TISSUE TUMOURS**

### **Bone tumours**

#### **Question**

How are bone tumours, e.g. osteosarcoma or Ewing sarcoma classified in the TNM system?

#### **Answer**

There is a TNM classification of bone tumours, see p. 153-156 of the TNM classification, 7th ed. [2].

## **SKIN TUMOURS**

### **Carcinoma of Skin**

#### **Question**

There are differences in the definitions of high-risk features of skin carcinoma between AJCC and UICC. How should these differences be handled?

#### **Answer**

For sake of uniformity, the UICC has adapted the AJCC criteria in a reprint of the TNM booklet, 7th ed. [2]. The differences are listed on p. 85 of the TNM Supplement. It is recommended to use the 2 mm size as a high-risk feature.

#### **Question**

Does the cartilage of the ear belong to 'deep extradermal structures?' For example, a 1.5 cm carcinoma of the skin of the ear with infiltration of the cartilage of the ear, should it be staged as T1 or T3?

#### **Answer**

The deep structures include cartilage (of the ear), and therefore the case should be classified as cT3/pT3 (see TNM Suppl. p. 85).

## **BREAST**

#### **Question**

If the clinical T has been determined by physical examination as well as by mammography and ultrasonography, which measurement is used for the cT? For instance: Tumour palpated as 3 cm, mammography shows 2 cm, is it T2 to T1?

#### **Answer**

According to a proposal in the TNM Supplement, the size for classification in this specific case is:  $0.5 \times 3.0 \text{ cm} + 0.5 \times 2.0 \text{ cm} = 2.5 \text{ cm}$  and thus T2 (see TNM Suppl. p. 90-91).

#### **Question**

Is there a TNM classification for carcinosarcomas of the breast or can we use the TNM classification of breast tumours?



**Answer**

In the TNM booklet 7th ed. [2] p. 182, it says: The classification applies to carcinomas and concerns the male as well as the female breast.

It is not applicable to carcinosarcomas.

**Question**

Are microscopic measurements of breast tumour size preferred to macroscopic measurement?

**Answer**

Microscopic measurement is preferred to macroscopic measurement because the estimation of a tumour margin macroscopically might not be precise enough.

**Question**

Should the rules of mathematics for rounding values be used? Should a tumour measuring 10.3 mm be rounded down to 1 cm and put in the pT1 b category or should this tumour be classified as pT1c?

**Answer**

The rules of mathematics should not be used. In this case the tumour should be classified as pT1c.

**Question**

Breast carcinoma 2.5 cm in diameter with invasion of the dermis/corium. Is this classified as pT2 or pT4?

**Answer**

The criteria for classifying a breast tumour cT4/pT4 include oedema, peau d'orange or ulceration of the skin of the breast and not invasion of the dermis. The tumour is classified as pT2 (see TNM Suppl. p. 89).

**Question**

Infiltrating lobular carcinoma, 3 x 2 x 1 cm, with extensive lymphovascular invasion. Pathology report: dermal lymphatics involved. Should this be classified as pT4d (inflammatory carcinoma)? There were no clinical physical examination data available.

**Answer**

Inflammatory carcinoma, cT4d, requires the macroscopic (clinical) features to be present. Microscopic involvement of dermal lymphatic vessels alone does not count for classification. Tumour is pT2 based on size (see TNM Suppl. p. 91).



**Question**

Clinically no palpable tumour, but a mammogram showing suspicious microcalcifications. Physical examination did not show a tumour. Surgical removal of the lesion was diagnosed carcinoma in situ, questionable microinvasion. How is this classified?

**Answer**

cT0: clinically no evidence of primary tumour.

pTis: carcinoma in situ. Questionable microinvasion leaves enough doubt to apply TNM rule no. 4: When in doubt choose the lower category (see TNM Suppl. p. 3).

**Question**

In tumours of the breast, how do we classify invasion of lymphatic vessels in paranodal fatty tissue of the axilla with and without involvement of the axillary lymph nodes?

**Answer**

Invasion of lymphatic vessels in the axilla is not considered in the TNM classification of breast tumours. The optional L (lymphatic) classification (p.17, TNM 7th ed.[2]) can be used to describe lymphatic vessel involvement (see TNM Suppl. p. 21).

**Question**

Regarding isolated tumour cell cluster definition in lymph nodes in breast carcinoma, if you have multiple clusters in a subcapsular sinus immediately adjacent to one another (spaced approximately 20 microns apart), but each measures less than 0.2 mm. Are these foci added up for the size or each considered separately in the measurement?

**Answer**

This issue has been frequently raised with the TNM helpdesk and generated considerable discussion. Strictly, these findings should be considered pN0(i+) and not micrometastasis. However, biology tells us that a classification of micrometastasis is more adequate. In these rare cases we recommend doing step sections and frequently find real micrometastasis or even macro metastasis.

**Question**

How does one classify an isolated tumour nodule in the axillary fat of a patient with breast carcinoma?

**Answer**

It should be classified as lymph node metastasis, if it has the form and smooth contour of a lymph node. A tumour nodule with an irregular contour may be classified as venous axillary invasion (V classification) (see TNM Suppl. p. 8).

**Question**

A 2.3 cm axillary lymph node had a small metastasis of cells 0.1 cm in size. How is that classified, according to the dimensions of the metastasis or to the dimensions of the lymph node?





**Answer**

The size used for classification is the size of the measured metastasis and not the size of the lymph node that contains the metastasis. The case would be classified as a micrometastasis ( $\leq 0.2$  cm) and coded pN1mi (see TNM Suppl. p. 9).

**Question**

In a case of Paget disease of the nipple with a small 0.3 cm tumour of the breast near the nipple, is this classified as pT1a or pT4?

**Answer**

This is classified pT1a. Paget disease associated with a tumour is classified according to the size of the tumour (TNM 7th ed., p. 184 [2]).

**Question**

How is microinvasive (<1 mm) breast cancer coded in the TNM?

**Answer**

It is coded as T1mi (see TNM Suppl. p. 89).

**Question**

How does one classify breast cancer after chemotherapy? Is pTpN appropriate?

**Answer**

'In those cases in which classification is performed during or following initial multimodality therapy, the cTNM or pTNM categories are identified by a y prefix' (TNM 7th ed. [2], p. 16). For example, ycT1N0M0 or ypT1N0 ycM0.

**Question**

The TNM Classification of Breast Tumours states: The clinical T1 category is further subclassified into T1mi, T1a, T1b, T1c.

There was a discussion among physicians here as to why this was included in the clinical description as microscopic invasion can only be defined pathologically.

**Answer**

Histologic examination is required on all clinical classifications for "confirmation of the disease". Pathologic classification, pT, requires more than histologic examination. It "requires the examination of the primary tumour with no gross tumour at the margins of resection" (see TNM 7th ed. [2]).

**Question**

What is the pT category and the R status of a 1.5 cm breast carcinoma detected histologically in the resection margin?

**Answer**

The pT category is pT1c and the R status R1 (see TNM Suppl. p. 89 and 15).





### Question

When a patient who had a hormonal therapy to the left breast cancer, has a new cancer in the right breast, should we use the prefix 'y' with this new cancer?

### Answer

The carcinoma of the right breast is classified without 'y'.

The 'y' symbol is used in those cases in which classification is performed during or following multimodality therapy (see p. 16-17 TNM booklet [2]).

### Question

How does one classify a breast tumour with invasion of the nipple/mamilla with or without ulceration?

### Answer

The nipple is not considered in the definitions of the T classification. Size and ulceration are relevant criteria for the T category.

Example:

Breast carcinoma 1.9 cm in diameter with invasion of the nipple

- With ulceration of the nipple cT4b/pT4b
- Without ulceration of the nipple cT1c/pT1c (see TNM Suppl. p. 91).

### Question

How do we classify a lymph node metastasis of breast cancer with a size of 1.8 mm and extension beyond the lymph node capsule?

### Answer

It should be classified as pN1mi, on the basis of its size. Extension beyond the capsule is no longer used as a criterion for pN classification.

### Question

I have a case of breast carcinoma where the sentinel node imprint shows carcinoma cells; however, after review of multiple levels, no malignant cells could be identified in the permanent sections from the sentinel lymph node. How do I classify the N category?

### Answer

This is indeed a difficult question. As the cytological demonstration (if this has not been an artefact) showed the existence of isolated tumour cells, I would propose classifying the case as pN0(sn)(i+) and documenting the case separately.



## **GYNAECOLOGICAL TUMOURS**

### **Cervix Uteri**

#### **Question**

For tumours of the cervix uteri, can we base the classification on the conisation for the establishment of the clinical TNM?

#### **Answer**

Conisation is a procedure that can be used to establish a clinical TNM classification in tumours of the cervix uteri. For details of when to use pTNM, see TNM Suppl. p. 157.

#### **Question**

How is the maximal horizontal spread measured in the squamous cell carcinoma of the cervix in case of multifocality? Do I measure the total extent of the lesion between the two lateral margins? Do I include only the largest tumour focus?

#### **Answer**

It is recommended to measure the total extent of the tumour foci and separately document the largest tumour focus as well as the number and size of other tumour foci.

In the TNM Supplement it says (p. 95): In the rare multifocal T1a tumours, for the horizontal spread FIGO classifies by the largest focus. This is in accordance with TNM Rule No. 5.

### **Corpus Uteri**

#### **Question**

I have a question regarding an endometrial adenocarcinoma of the corpus uteri infiltrating beyond the inner half of the myometrium and presenting with positive cytology. According to the old (6th ed.) classification, this situation would be staged pT3a. According to the new classification, staging changed to pT1b (FIGO IB) and the positive cytology is no longer included in the T category. How are these findings reflected in considerations for (radio)therapy?

#### **Answer**

The staging has changed and the case is classified as pT1b (stage IB) if the lymph nodes are negative and there are no distant metastases.

Positive peritoneal cytology 'per se' does not change the stage as defined by the pathological evaluation of T and N, but is considered in the M classification (M1 (cy +)) (see TNM Suppl. p. 11).

As for the adjuvant therapy, it is not a UICC or FIGO commitment to recommend how and when to deliver post-surgical treatment. This should be indicated according to protocols of a single institution.



**Question**

A uterine corpus tumour extends into the parametrium. Should it be classified as T2 or T3a?

**Answer**

T3b. T2 tumours invade the cervix but do not extend beyond the uterus (see TNM Suppl. p. 96).

**Question**

Serous adenocarcinoma of the endometrium T1b with extensive lymph vessel invasion and omental metastatic serous adenocarcinoma is present. Does this qualify as cM1/pM1?

**Answer**

This case is classified as pT1bpM1 and the lymph node status should be added. Note that lymphatic vessel invasion is neither considered in the T categories nor in the N categories but can be included in the optional descriptor L.

**Question**

A radical hysterectomy specimen shows an adenocarcinoma penetrating the serosal surface (pT3a) of the corpus uteri. All regional lymph nodes were negative, but there was metastatic adenocarcinoma in parametrial soft tissue. Does this change the stage of the tumour?

**Answer**

Discontinuous parametrial involvement is classified cT3b/pT3b (see TNM Suppl. p. 96).

**Question**

I received a hysterectomy specimen with both adnexae operated for endometrial carcinoma. The fallopian tubes have malignant glands floating in the lumen (however, the fallopian tubes themselves are not involved). Will the case be staged as pT3a?

**Answer**

As the floating tumour cells may be artificial and show no signs of invasion, they should not be considered in the TNM classification of endometrial carcinoma. Thus, the classification depends only on the extent of the carcinoma in the uterus.

**Question**

Primary endometrial carcinoma of the corpus uteri with direct invasion (per continuitatem) into the small bowel wall and the omentum majus. How is this classified, pT4 or pM1 ?

**Answer**

If endometrial carcinoma directly invades bowel wall (small bowel or large bowel) as well as omentum, this is classified as pT4.

**Question**

Endometrial carcinoma of the corpus uteri with metastases in the omentum. Is this classified as pT4 or pM1?



**Answer**

Omental foci (discontinuous from the primary tumour) are considered distant metastasis = cM1/pM1

**Ovary versus Uterus**

**Question**

A patient has a high-grade (serous and clear cell) carcinoma confined to endometrium with peritoneal implants including the surface of both ovaries, a small focus in one ovary and a large omental cake. Should we stage this as an ovarian tumour (M0) or an endometrial tumour (M1)?

**Answer**

It would be very unusual for a superficial endometrial primary to produce an omental mass. Most would treat this as a primary ovarian lesion with a superficial second primary in the endometrium, making it a Stage IIIC ovarian with a Stage IA endometrial tumour.

**Ovary**

**Question**

A patient has a primary ovarian cancer. Ovaries were not removed. Laparotomy shows a 2 cm epiploic metastasis of papillary serous adenocarcinoma. Should I stage this tumour, cT3b or pT3b, or something else?

**Answer**

Even though the ovaries were not removed, if you have microscopic confirmation of a 2 cm peritoneal metastasis outside the pelvis, pT3b is correct (see TNM Suppl. p. 99).

**Question**

What pathological T category does the presence of omental metastases confer in an ovarian carcinoma? What about metastases to the rectosigmoid pericolic fat?

**Answer**

The classification of omental metastasis is summarized below (see TNM Suppl. p. 98). Invasion or metastasis of the rectosigmoid pericolic fat would be classified as cT2b/pT2b.

<b>UICC FIGO 1988</b>		
T3 and/or N1	III	Tumour involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis and/or regional lymph node metastasis
T3a	IIIA	Microscopic metastasis beyond pelvis
T3b	IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less
T3c	IIIC	Macroscopic peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis



### **Question**

An ovarian carcinoma with peritoneal dissemination and involvement of the sigmoid colon with a lymph node metastasis in the sigmoid lymph nodes. How do I classify this case?

### **Answer**

The lymph nodes of an infiltrated adjacent organ are considered as those of the primary site for N classification ; hence regional in this case. Therefore, this case should be classified as pT3c pN1 cM0 (see TNM Suppl. p. 7).

### **Question**

I have a case with a bilateral ovarian serous surface borderline tumour. There are microscopic non-invasive epithelial implants in the omentum. Do this implants make the case a Stage III?

### **Answer**

The TNM classification applies to malignant ovarian neoplasms of both epithelial and stromal origin including those of borderline malignancy or of low malignant potential.

Neither the FIGO classification nor the UICC/AJCC TNM classification in their 6th and 7th ed. make a difference between non-invasive or invasive implants in the omental fat.

Therefore, the case you describe should be classified as pT3a (FIGO IIIA).

It is recommended to document these cases separately to get more information on possible different outcomes.

## **UROLOGICAL TUMOURS**

### **Prostate**

#### **Question**

During a radical prostatectomy for transitional cell carcinoma, if we find a clinically unexpected bilateral prostatic adenocarcinoma should we consider it as incidental (pT1) or as a pT2 tumour?

#### **Answer**

At least pT2c. Note : pT1 does not exist for prostate tumours (see TNM Suppl. p. 102).

#### **Question**

How do we classify perineural spread of prostatic carcinoma in extracapsular tissue?

#### **Answer**

pT3a because of the extracapsular spread of the tumour. In addition to the pT category, the perineural invasion can be indicated by the optional descriptor Pn (Pn1).



### **Question**

If a patient has had biopsies showing different Gleason grades in different biopsy specimens, how is the overall Gleason score reported? Does the TNM system follow the 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason grading in prostatic adenocarcinoma recommendation? That is, that the highest individual Gleason score is designated the overall Gleason score?

### **Answer**

The TNM system recommends use of the International Society of Urological Pathology (ISUP) and College of American Pathologists (CAP) standard, which is to report the Gleason score with primary and secondary grades for each site separately [13].

### **Question**

If the biopsies are positive in both lobes (right and left) of the prostate, but in only one lobe a nodule is seen on transrectal ultrasonography and palpable. Do I classify this as a cT2a/b or cT2c situation?

### **Answer**

I would classify this as cT2a.

## **Testis**

### **Question**

I have a testicular tumour that is invading into the epididymis and into the perihilar fat. There is lymphovascular invasion. It does not extend into the tunica vaginalis. Does the fat at the hilum count as spermatic cord or not?

### **Answer**

The perihilar fat is considered part of the spermatic cord, and therefore the case you describe is classified as pT3 (see TNM Suppl. p. 105).

## **Kidney**

### **Question**

We resected a renal cell carcinoma. Histology showed a small focus of tumour in the peripelvic fat and tumour invasion into blood vessels. What would be the T category?

### **Answer**

Invasion of the peripelvic fat would place this case into pT3a category. Histological identification of blood vessel involvement does not justify pT3b as this specifically requires grossly visible invasion (see p. 256, TNM 7th ed. [2]).

### **Question**

Gross invasion of the renal vein in kidney cancer - is this classified as pT3b and how is 'gross' defined?



### **Answer**

In contrast to the 6th ed. (pT3b), in the 7th ed. extension of a tumour in the renal vein or its segmental (muscle containing) branches is classified as pT3a. “Gross” corresponds to macroscopically visible (see TNM Suppl. p. 105).

### **Question**

How kidney cancer is staged, which invades the renal sinus fat?

### **Answer**

A renal cell carcinoma invading the renal sinus fat (peripelvic fat) is classified cT3a/pT3a, corresponding to Stage III if there are no distant metastases.

### **Question**

In the TNM classification for renal cell carcinoma, a tumour that involves ipsilateral adrenal gland is classified as T4. What about spread to the contralateral kidney and/or adrenal gland (M1)?

### **Answer**

Direct spread to the contralateral adrenal gland as well as to contralateral kidney is M1 (see TNM Suppl. p. 106). If both kidney's show a separate tumour, both kidney's need a separate TNM classification.

### **Question**

Spread of a kidney tumour to the lumen of the renal pelvis and free-floating tumour tissue in the ureter-what will be the T category?

### **Answer**

The described findings of tumour in the renal pelvis or ureter are not considered in the T category of the kidney tumours.

## **Renal pelvis and ureter**

### **Question**

What pT category should be considered for urothelial carcinoma of renal pelvis and calyces with superficial invasion to parenchyma of renal papilla?

### **Answer**

cT3/pT3 for renal pelvis is defined as tumour invasion beyond muscularis into peripelvic fat or renal parenchyma. According to that definition, your case classified as pT3.

## **Bladder**

### **Question**

For carcinoma of the bladder, if there is involvement of the seminal vesicle should it be regarded as pT4a?



### **Answer**

If the wall of the seminal vesicle or stroma of the prostate is involved, it should be T4a. If there is only in situ carcinoma in the seminal vesicle, it should not be classified T4. There are data that carcinoma in situ in the prostatic ducts does not adversely impact survival [14]. (see TNM Suppl. p. 108).

### **Question**

For carcinoma of the bladder, if there is invasion of the prostate by extension of the urethra, is this classified as T3 or T4?

### **Answer**

A cT4/pT4 bladder carcinoma is diagnosed if there is a direct invasion of the prostatic stroma (glands are not sufficient to classify as T4). The extension of an In situ component does not qualify for cT4/pT4. There are data that CIS in the prostatic ducts does not adversely impact survival [14] (see TNM Suppl. p. 108).

### **Question**

How do I classify a carcinoma of bladder with invasion of the abdominal cavity and perhaps invasion of small or large bowel?

### **Answer**

I may refer you to the TNM Supplement, p. 108: Direct invasion of the large and small intestine by a bladder tumour should be classified as cT4a/pT4a. The same applies to an invasion through the peritoneum covering the bladder.

### **Question**

A small cell carcinoma of bladder with metastases in common iliac and para-aortic lymph nodes. Is this case classified as pN3pM1?

### **Answer**

Metastasis in common iliac lymph nodes are classified as cN3/pN3 and metastasis in para-aortic lymph nodes are classified as cM1/pM1 (see TNM Suppl. p. 126).

## **Urethra**

### **Question**

Urothelial carcinoma with extension along urethral mucosa to the skin of the glans penis (pagetoid extension within epidermis of the skin of glans). What would be the TNM stage? The tumour itself was in situ within the urethra.

### **Answer**

The extension as a carcinoma in situ does not change the T category or the stage. Additionally, in carcinoma in situ no regional lymph node metastases are to be expected.





## REFERENCES

1. Hermark P, Hutter RVP, Sobin LH, Wittekind C., *Classification of Isolated (Disseminated, Circulating) Tumour Cells and Micrometastasis*. *Cancer* 1999; 86:2668-2673.
2. Sobin LH., Gospodarowicz MK, Wittekind Ch (eds), *TNM Classification of Malignant Tumours*, 7<sup>th</sup> ed..Oxford: Blackwell Publishing, 2010.
3. *UICC (International Union Against Cancer) TNM Classification of Malignant Tumours*. 6th ed.. Sobin LH, Wittekind Ch., eds. New York: Wiley; 2002.
- 4.Ohkagi H, Reifenberger G, Nomura K, et al. *Brain Tumours: Gliomas*. In Gospodarowicz MK, Henson DE, Hutter RVP, et al. (eds) *UICC Prognostic Factors in Cancer*. 2nd ed.. Wiley Liss: New York, pp. 725-743.
5. *AJCC Cancer Staging Manual*. 7th ed.. Edge SB, Byrd DR, Compton CC, Fritz AG, et al. (eds) New York: Springer; 2009.
6. McCaughey WT, Schryer MJ, Lin X, et al. *Extraovarian pelvic serous tumour with marked calcification*. *Arch Pathol Lab Med* 1986; 110:78-80.
7. Killackey MA, Davies AR. *Papillary serous carcinoma of the peritoneal surface: matched-case comparison with papillary serous ovarian carcinoma*. *Gynecol Oncol* 1993; 51:171-174.
8. *FIGO Annual Report 24th on the Results of Treatment in Gynecological Cancer*. Pecorelli S, Beller U, Heintz APM, et al. *Epidermiol Biostatist* 2001;vol. 6:1-184.
9. Som PM, Curtin HD (2003) *Fascia and spaces of the neck*. In Som PM, Curtin HD (eds) *Head and Neck Imaging*. 4th ed.. Mosby, St. Louis, pp. 1805-1827.
10. *UICC (International Union Against Cancer) TNM Supplement. A Commentary on Uniform Use*. 3rd ed.. Wittekind Ch, Henson DE, Hutter RVP, et al., eds. New York: Wiley; 2003.
11. *UICC (International Union Against Cancer) TNM Classification of Malignant Tumours*, 4th ed., 2nd revision. Hermanek P, Sobin LH, eds. Berlin, Heide(berg, New York: Springer; 1992.
12. *UICC (International Union Against Cancer) TNM Classification of Malignant Tumours*. 5th ed.. Sobin LH, Wittekind Ch, eds. New York: Wiley; 1997.
13. Srigle JR. *Personal communication*. 2010.
14. Montie J E, Wojno K, Klein E, et al. *Transitional cell carcinoma in situ of the seminal vesicles: 8 cases with discussion of pathogenesis, and clinical and biological implications*. *J Urol* 1997; 158:1895-1898.